

## PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING  
AMENDMENTS OF THE CLAIMS(PCT Rule 62 and  
Administrative Instructions, Section 417)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

21 August 2000 (21.08.00)

in its capacity as International Preliminary Examining Authority

International application No.

PCT/IL99/00619

International filing date (day/month/year)

17 November 1999 (17.11.99)

Applicant

BIOSOMA LTD. et al

The International Bureau hereby informs the International Preliminary Examining Authority that no amendments under Article 19 have been received by the International Bureau (Administrative Instructions, Section 417).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Nestor Santesso

Telephone No. (41-22) 338.83.38

## P/ INT COOPERATION TREA

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

COLB, Sanford, T.  
Sanford T. Colb & Co.  
P.O. Box 2273  
76122 Rehovot  
ISRAËL

Date of mailing (day/month/year) 23 October 2000 (23.10.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 36077	
International application No. PCT/IL99/00619	International filing date (day/month/year) 17 November 1999 (17.11.99)

1. The following indications appeared on record concerning: <input checked="" type="checkbox"/> the applicant <input type="checkbox"/> the inventor <input type="checkbox"/> the agent <input type="checkbox"/> the common representative		
Name and Address BIOSOMA LTD. 5 Safir Street Ramat Gan 52622 Israel	State of Nationality IL	State of Residence IL
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning: <input type="checkbox"/> the person <input checked="" type="checkbox"/> the name <input checked="" type="checkbox"/> the address <input checked="" type="checkbox"/> the nationality <input checked="" type="checkbox"/> the residence		
Name and Address FERRING BV Polaris Avenue 144 NL-2132 JX Hoofddorp Netherlands	State of Nationality NL	State of Residence NL
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to: <input checked="" type="checkbox"/> the receiving Office <input type="checkbox"/> the designated Offices concerned <input type="checkbox"/> the International Searching Authority <input checked="" type="checkbox"/> the elected Offices concerned <input checked="" type="checkbox"/> the International Preliminary Examining Authority <input type="checkbox"/> other:		

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer J. Leitao Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

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## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 21 August 2000 (21.08.00)	
<b>International application No.</b> PCT/IL99/00619	<b>Applicant's or agent's file reference</b> 36077
<b>International filing date (day/month/year)</b> 17 November 1999 (17.11.99)	<b>Priority date (day/month/year)</b> 18 November 1998 (18.11.98)
<b>Applicant</b> JOSSIOFF, Azariah	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
19 June 2000 (19.06.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer</p> <p>Nestor Santesso</p> <p>Telephone No.: (41-22) 338.83.38</p>
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**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>7</sup> :</b> <b>A61K 9/02, 9/20, 9/46</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 00/28970</b> <b>(43) International Publication Date:</b> 25 May 2000 (25.05.00)
<b>(21) International Application Number:</b> PCT/IL99/00619 <b>(22) International Filing Date:</b> 17 November 1999 (17.11.99)  <b>(30) Priority Data:</b> 127129 18 November 1998 (18.11.98) IL  <b>(71) Applicant (for all designated States except US):</b> BIOSOMA LTD. [IL/IL]; Safir Street 5, 52622 Ramat Gan (IL).  <b>(72) Inventor; and</b> <b>(75) Inventor/Applicant (for US only):</b> JOSSISOFF, Azariah [IL/IL]; Safir Street 5, 52622 Ramat Gan (IL).  <b>(74) Agents:</b> COLB, Sanford, T. et al.; Sanford T. Colb & Co., P.O. Box 2273, 76122 Rehovot (IL).		<b>(81) Designated States:</b> AE, AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), DM, EE, EE (Utility model), ES, FI, FI (Utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> VAGINALLY ADMINISTRABLE PROGESTERONE-CONTAINING TABLETS AND METHOD FOR PREPARING SAME		
<b>(57) Abstract</b>  There is provided a method for preparing a tablet for the vaginal administration of progesterone for systemic use, comprising the steps of: slowly mixing water with micronized progesterone, the total amount of water mixed with said micronized progesterone not exceeding the maximum wetting capacity of the micronized progesterone, whereby to obtain wetted micronized progesterone; drying said wetted, micronized progesterone to a humidity content of substantially 0 %, whereby to form substantially dry micronized progesterone; mixing said substantially dry micronized progesterone with other pharmaceutically acceptable excipients or diluents therefor; and forming a tablet by direct compaction of said substantially dry micronized progesterone which has been mixed with said other pharmaceutically acceptable excipients or diluents therefor. Tablets so prepared, as well as a tablet comprising between about 6 to 20 wt.% progesterone and between about 5 to 12 wt.% effervescent, are also provided.		

**FOR THE PURPOSES OF INFORMATION ONLY**

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EE	Estonia						

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IL.99/00619

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 9/02, 9/20, 9/46

US CL : 424/430, 433, 464, 466

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/430, 433, 464, 466

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,084,277 A (GRECO et al) 28 January 1992, see examples 1, 2 and 14.	1-7 and 40-45
Y	US 5,116,619 A (GRECO et al) 26 May 1992, see examples 1, 2 and 14.	1-7 and 40-45

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

25 FEBRUARY 2000

Date of mailing of the international search report

14 MAR 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

JAMES M. SPEAR

Telephone No. (703) 308-1235

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IL99/00619

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 8-39  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

REC'D 07 DEC 2000

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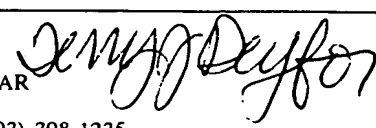
# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 6727/2H326-WO	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IL99/00619	International filing date (day/month/year) 17 NOVEMBER 1999	Priority date (day/month/year) 18 NOVEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): A 61K 9/02, 9/20, 9/46 and US Cl.: 424/430, 433, 464, 466		
Applicant BIOSOMA LTD.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets.  
☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
 These annexes consist of a total of 0 sheets.
- This report contains indications relating to the following items:
  - ☒ Basis of the report
  - ☐ Priority
  - ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
  - ☐ Lack of unity of invention
  - ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - ☐ Certain documents cited
  - ☐ Certain defects in the international application
  - ☐ Certain observations on the international application

Date of submission of the demand 19 JUNE 2000	Date of completion of this report 31 AUGUST 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer JAMES M. SPEAR 
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235



## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/IL99/00619

**I. Basis of the report****1. With regard to the elements of the international application: \***☒ the international application as originally filed☒ the description:

pages 1-16 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the claims:

pages 17-24 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the drawings:

pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:

pages NONE , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☒ The amendments have resulted in the cancellation of:**

- ☒ the description, pages NONE  
☒ the claims, Nos. NONE  
☒ the drawings, sheets/fig NONE

**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/IL99/00619

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 8-39

because:

☐ the said international application, or the said claim Nos. \_ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. \_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 8-39.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/IL99/00619

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. statement

Novelty (N)

Claims	<u>1-7 and 40-45</u>	YES
Claims	<u>NONE</u>	NO

Inventive Step (IS)

Claims	<u>1-7 and 40-45</u>	YES
Claims	<u>NONE</u>	NO

Industrial Applicability (IA)

Claims	<u>1-7 and 40-45</u>	YES
Claims	<u>NONE</u>	NO

## 2. citations and explanations (Rule 70.7)

Claims 1-7 and 40-45 meet the criteria set out in PCT Articles 33(2)-(4), because the prior art does not teach or fairly suggest applicant's method and vaginal tablet produced by said method wherein conventional granulation is not required. The prior art does not show applicant's method of formulating progesterone having bulk properties that normally render it unsuitable for direct compaction into vaginal tablets having effective concentrations for therapeutic use. Applicant further shows a means for incorporating an effervescent into said vaginal tablet. Applicant's method of mixing micronized progesterone with water to provide a wetted micronized progesterone then drying said wetted micronized progesterone prior to further processing and compaction results in a tablet for vaginal administration having distinct properties.

The vaginal tablets are useful in medicine because applicant's process utilizing compaction produces tablets that are more economical than prior art progesterone vaginal tablets and further provides a means for utilizing an effervescent in a vaginal tablet for optimum dissolution and absorption of progesterone.

----- NEW CITATIONS -----  
NONE